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(54) Title: SOLID-PHASE FLUORINATION OF BENZOTHAZOLES



(57) Abstract: The invention provides a process for the production of an <sup>18</sup>F-labelled tracer which comprises treatment of a solid support-bound precursor of formula (I) SOLID SUPPORT-LINKER- X -TRACER (I) wherein X is a group which promotes nucleophilic substitution at a specific site on the attached TRACER and the TRACER is of formula (A).

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05574

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K51/04 C07B59/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SUTCLIFFE-GOULDEN J L ET AL: "Solid phase synthesis of [F]Labelled peptides for positron emission tomography" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 10, no. 14, 17 July 2000 (2000-07-17), pages 1501-1503, XP004209688 ISSN: 0960-894X page 1502, column 2; figure 1 abstract	1-5,8,14
Y	WO 02/070020 A (UNIV WESTERN ONTARIO) 12 September 2002 (2002-09-12) abstract; claims 1,6,19,22 page 3, lines 10-15; claim 1 page 15, lines 24,25	1-5,10,12,14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

29 March 2004

Date of mailing of the international search report

23 JUL 2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05574

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99/18053 A (HUNTER DUNCAN H ;ZHU XIZHEN (CA); UNIV WESTERN ONTARIO (CA)) 15 April 1999 (1999-04-15) page 3; claim 1	1-5
X	----- US 4 540 648 A (SCHELER SIEGFRIED) 10 September 1985 (1985-09-10) abstract; claim 2 column 7, paragraph 2; claim 1	9
Y	----- LABROO V M ET AL: "DIRECT ELECTROPHILIC FLUORINATION OF TYROSINE IN DERMORPHIN ANALOGUES AND ITS EFFECT ON BIOLOGICAL ACTIVITY RECEPTOR AFFINITY AND SELECTIVITY" INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, vol. 37, no. 5, 1991, pages 430-439, XP008029035 ISSN: 0367-8377 page 430, column 1 page 433, column 2, paragraph 1	1-5,8
Y	----- WO 01/14354 A (HUTCHINSON IAN PAUL ;POOLE TRACEY DAWN (GB); WESTWELL ANDREW DAVID) 1 March 2001 (2001-03-01) route D page 18; claims 17,25,25; examples 44,45	1-5,8,9
Y	----- WO 02/16333 A (MATHIS CHESTER A JR ;KLUNK WILLIAM E (US); UNIV PITTSBURGH (US); W) 28 February 2002 (2002-02-28) see structure Dclaims 1,2,26,34	1-5,8,9, 14
A	----- WO 97/42203 A (LAURICELLA BENJAMIN P ;LEMAIRE CHRISTIAN F (BE); LUXEN ANDRE (BE);) 13 November 1997 (1997-11-13) claims 1,24	10,12
A	----- US 5 312 592 A (ANDERSSON HENRY) 17 May 1994 (1994-05-17) claim 3	10,12
P,X	----- WO 03/002157 A (GIBSON ALEXANDER MARK ;IMAGING RES SOLUTIONS LTD (GB); BRADY FRANK) 9 January 2003 (2003-01-09) page 4; claims 1,13-15	1-5,8-14
P,Y	----- WO 03/002489 A (IMAGING RES SOLUTIONS LTD ;BRADY FRANK (GB); AMERSHAM PLC (GB); LU) 9 January 2003 (2003-01-09) claims 7,8; example 3	1-5,8-14
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05574

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	WO 03/068269 A (IMAGING RES SOLUTIONS LTD ;BRADY FRANK (GB); AMERSHAM PLC (GB); WI) 21 August 2003 (2003-08-21) claims 7,8; examples 3,4 -----	1-5,8-14

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/05574

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim 14 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: partially 1-5, 8-14  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-5 (complete) ; 8-14 (partially)

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claim 14 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box I.2

Claims Nos.: partially 1-5, 8-14

Present claims 1-5, 8-14 as far as related to the first invention relate to an extremely large number of possible compounds/chemical groups defined as "a group which promotes nucleophilic substitution" (claim 1); "a linker" (claims 1-5); "a protecting group" (claims 1-5).

Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/chemical groups claimed.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds explicitly disclosed by chemical name in claims 2-5 excluding the vague term "protecting group" and those linkers mentioned in the description at pages 6, lines 10-page 7, line 5 and protecting groups at page 7, line 15- page 8, line 2.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5 complete; 8-14 partially

A process for the production of an 18F labelled tracer which comprises treatment of a solid support-bound precursor of formula I with 18F to produce the labelled tracer of formula II as depicted in claim 1. The compound of formula Ia per se. Pharmaceutical kit and cartridge for the preparation of said 18F labelled tracer of formula II. Use of the kit or cartridge in positron emission tomography (PET). Excluding the subject matter of invention 2.

1.1. claims: 2,3 complete; 1, 8-14 partially

A process for the production of an 18F labelled tracer which comprises treatment of a solid support-bound precursor of formula Ia with 18F to produce the labelled tracer of formula IIa as depicted in claim 2. The compound of formula Ia per se. Pharmaceutical kit and cartridge for the preparation of said 18F labelled tracer of formula IIa. Use of the kit or cartridge in positron emission tomography (PET).

1.2. claims: 4, 5 complete; 1, 8-14 partially

A process for the production of an 18F labelled tracer which comprises treatment of a solid support-bound precursor of formula Ib with 18F- to produce the labelled tracer of formula IIb as depicted in claim 4. The compound of formula Ib per se. Pharmaceutical kit and cartridge for the preparation of said 18F labelled tracer of formula IIb. Use of the kit or cartridge in positron emission tomography (PET).

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2. claims: 6, 7 complete; 8-14 partially

A process for the production of an 18F labelled tracer which comprises treatment of a solid support-bound precursor of formula III with a source of 18F to produce the labelled tracer of formula IV as depicted in claim 6. The compound of formula III per se. Pharmaceutical kit and cartridge for the preparation of said 18F labelled tracer of formula IV. Use of the kit or cartridge in positron emission tomography (PET). Excluding the subject matter of invention 1

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/05574

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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